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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/478,977 | 01/06/2000 | PETER C. BROOKS | 13761-727 | 2450 |

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| EXAMINER | |
|---|---|
| HARRIS, ALANA M | |
| **ART UNIT** | **PAPER NUMBER** |
| 1642 | |

DATE MAILED: 11/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/478,977 | BROOKS ET AL. | |
| | Examiner | Art Unit | |
| | Alana M. Harris, Ph.D. | 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *16 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-4,6,10-18,20-25,27-30,32-34,36-38 and 40-73* is/are pending in the application.

4a) Of the above claim(s) *20-25,27-30,32-34,36-38,40-64 and 66* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,10,12,16-18,65 and 67-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *08/03/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Response to Amendments and Arguments*

1. Claims 1-4, 6, 10-18, 20-25, 27-30, 32-34, 36-38 and 40-73 are pending.

Claims 1 and 65-67 have been amended.

Claims 65-73 have been added.

Claims 11 and 13-15 have been cancelled.

Claims 20-25, 27-30, 32-34, 36-38, 40-64 and 66, drawn to non-elected inventions are withdrawn from examination.

Claims 1-4, 6, 10, 12, 16-18, 65 and 67-73 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### *Priority*

3. Provisional documents 60/114,877 (filed January 6, 1999), 60/114,878 (filed January 6, 1999), 60/152,496 (filed September 2, 1999) and 60/143,534 (filed July 13, 1999) from which Applicants request priority benefit were reviewed by the Examiner. Claims 1-4, 6, 10, 16-18, 65, 66 and 68-73 are afforded the effective filing date of January 6, 1999.

***Withdrawn Objection***

***Specification***

4. The disclosure is no longer objected to because on page 3, line 16 the term "effect" was replaced with the term "affect".

***Withdrawn Rejections***

***Claim Rejections - 35 USC § 112***

5. The rejection of claim 11 under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure without complete evidence either that the claimed biological materials are known and readily available to the public or complete evidence of the deposit of the biological materials is withdrawn in light of the cancellation of the claim.

6. The rejection of claims 1-4, 6, 10, 12 and 16-18 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been withdrawn. Claims 11 and 13-15 have been cancelled.

***Claim Rejections - 35 USC § 102***

7. The rejection of claims 1-4 and 6 under 35 U.S.C. 102(b) as being anticipated by Brooks et al. (J. Clin. Invest. 96: 1815-1822, October 1995/ IDS reference C2, Paper

number 9), as evidenced by Brooks et al. (Cell 85: 683-693, May 31, 1996) is withdrawn in light of Applicatns' arguments.

8. The rejection of claim 11 under 35 U.S.C. 102(a) as being anticipated by Petitclerc et al. (Cancer Research 59:2724-2730, June 1, 1999) is withdrawn in light of the cancellation of the claim.

***New Grounds of Rejection***

***Claim Rejections - 35 USC § 112***

9. Claims 65 and 66 are rejected under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure without complete evidence either that the claimed biological materials are known and readily available to the public or complete evidence of the deposit of the biological materials.

In anticipation of the instant rejection Applicants state the specification provides adequate written description and enabling disclosure of the two monoclonal antibodies, HU177 and XL313, which are claimed by their binding specificity to a particular antigen, denatured collagen-type I. Applicants have pointed out that the Examiner appears to present contradictory information. All of these points of view and argument have been carefully considered, but found unpersuasive.

Exact replication of an antibody capable of binding a specific epitope is an unpredictable event. Although applicant has provided a written description of a method for generating and isolating the specified monoclonal antibodies, this method will not

necessarily reproduce antibodies and which are chemically and structurally identical to those claimed. It is unclear that one of skill in the art could derive antibodies identical to those claimed. Undue experimentation would be required to screen all of the possible antibody species to obtain the claimed antibodies.

Because one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed in the absence of the availability of the claimed antibodies, a suitable deposit of the molecules designated as HU177 and XL313 for patent purposes, evidence of public availability of the claimed cell lines or evidence of the reproducibility without undue experimentation of the claimed cell lines, is required.

Applicants have not made a referral to the deposit of the antibodies in the specification. There is insufficient assurance that all required deposits have been made and all the conditions of 37 CFR 1.801-1.809 met.

If the deposits are made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposits have been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

***Claim Rejections - 35 USC § 102***

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

11. Claims 1-4, 6, 10, 12, 65 and 67-70 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent 5,972,623 (filing date July 31, 1997). U.S. Patent #5,972,623 discloses monoclonal antibody 10B1 which strongly binds type I $\alpha$1 helicopeptide I in single-stranded form, but does not cross react with intact collagen of type I and does not react to a significant extent with an epitope in intact, triple helical collagen, see column 8, lines 26-54. The antibody has a binding affinity for the epitope sequence in triple helical collagen that is at least 10-fold less and absent evidence to the contrary this monoclonal antibody has the same binding specificity of monoclonal antibodies, HU177 and XL313. "Example 5 [of the patent] describes a procedure to produce polyclonal

antibodies against the helicopeptide I.", see column 7, lines 51-67 and column 17, lines 29-53.

12. Claims 1-4, 6, 10, 65 and 67-69 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent number 5,320,970 (issued June 14, 1994/ IDS reference submitted August 30, 2004). U.S. Patent #5,320,970 discloses monoclonal antibody 1H11 which specifically recognized type I collagen telopeptide fragments created by protease treatment, see column 6, lines 49-68, Formula III (type I collagen, alpha) ; column 7, lines 27-41; column 10, lines 46 and 47. Absent evidence to the contrary this monoclonal antibody has the same binding specificity of monoclonal antibodies, HU177 and XL313, as well as having reduced affinity to native triple helical form of collagen type-I.

***Claim Rejections - 35 USC § 103***

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 1-4, 6, 10, 12, 16-18, 65 and 67-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent number 5,972,623 (filing date July 31, 1997), in view of U.S. Patent number 5,530,101 (issued June 25, 1996). The teachings of U.S. Patent #5,972,623 have been presented in the 102(e) rejection of paragraph number

11. Patent '623 does not teach wherein the antibody antagonist is a humanized or chemically modified monoclonal antibody, a fragment of a monoclonal antibody or conjugated to cytotoxic agents.

However, U.S. Patent #5,530,101 teaches a method of producing humanized antibodies, polypeptide fragments comprising only a portion of the primary antibody structure and a variety of cytotoxic agents combined with antibodies. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to produce humanized antibodies with strong affinity to a predetermined antigen, see column 2, lines 25-27. One of ordinary skill in the art would have been motivated to manufacture humanized/chemically modified monoclonal antibody, fragments of a monoclonal antibody and conjugates to a cytotoxic or cytostatic agents with a reasonable expectation of success by teachings in the recited patents because these antibodies can be made with relative ease and have diagnostic utilities, applicability in numerous types of immunoassays and can be administered for prophylactic and/or therapeutic treatments, see patent '101, columns 19 and 20; column 26, lines 25-30; column 28, lines 51-53; patent '623, Example 12 of bridging columns 22 and 23.

15. Claims 1-4, 6, 10, 16-18, 65, 67-69 and 71-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent number 5,320,970 (issued June 14, 1994/ IDS reference submitted August 30, 2004), in view of U.S. Patent number 5,530,101 (issued June 25, 1996) and U.S. Patent number 5,972,623 (filing date July

31, 1997). The teachings of U.S. Patent #5,320,910 have been presented in the 102(e) rejection of paragraph number 12. Patent '910 does not teach wherein the antibody antagonist is a polyclonal antibody, humanized or chemically modified monoclonal antibody, a fragment of a monoclonal antibody or conjugated to cytotoxic agents.

However, U.S. Patent #5,530,101 teaches a method of producing humanized antibodies, polypeptide fragments comprising only a portion of the primary antibody structure and a variety of cytotoxic agents combined with antibodies. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to produce humanized antibodies with strong affinity to a predetermined antigen, see column 2, lines 25-27. One of ordinary skill in the art would have been motivated to manufacture humanized/chemically modified monoclonal antibody, fragments of a monoclonal antibody and conjugates to a cytotoxic or cytostatic agents with a reasonable expectation of success by teachings in the recited patents because these antibodies can be made with relative ease and have diagnostic utilities, applicability in numerous types of immunoassays and can be administered for prophylactic and/or therapeutic treatments, see patent '101, columns 19 and 20; column 26, lines 25-30; column 28, lines 51-53.

However, U.S. Patent #5,972,623 teaches a method of producing polyclonal antibodies having binding specificity for denatured collagen type I, see column 4, lines 23-29; column 7, lines 51-67; and column 17, lines 29-52. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to implement the methodology of patent '623 to manufacture polyclonal antibody

antagonists. One of ordinary skill in the art would have been motivated to manufacture these types of antagonists because it is art known that polyclonal antibodies have been used to assist in specific characterization of proteins and to validate gene targets at protein level. In addition, these antibodies may be useful in diagnostic and therapeutic applications for many diseases.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571) 272-0831. The examiner works a flexible schedule, however she can normally be reached between the hours of 6:30 am to 5:30 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER

Alana M. Harris, Ph.D.

28 October 2004